

18 19 20

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

ring/chain nodes :

21

chain bonds :

15-19 16-20 17-18 20-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-15 8-9 8-17 9-10 9-11 10-14

11-12 12-13 13-14 15-16 16-17

exact/norm bonds :

1-2 1-6 2-3 3-4 4-5 7-15 8-17 15-16 15-19 16-17 17-18

exact bonds :

16-20 20-21

normalized bonds :

5-6 5-7 6-10 7-8 8-9 9-10 9-11 10-14 11-12 12-13 13-14

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS

20:CLASS 21:CLASS

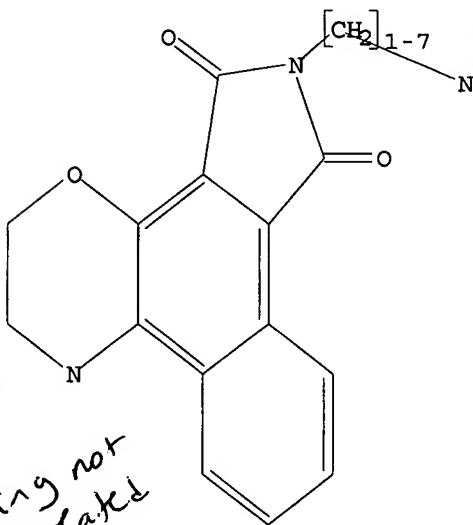
Broad search

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 08:12:27 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 0 TO 0
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 08:12:36 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.01

L3 11 SEA SSS FUL L1

=> file caplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 172.10 | 172.31 |

FILE 'CAPLUS' ENTERED AT 08:12:41 ON 21 MAY 2007
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FILE LAST UPDATED: 20 May 2007 (20070520/ED)

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=> s l3

L4 1 L3

=> d ibib abs hitstr tot

OWN
WORK

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER:

2004:329922 CAPLUS

DOCUMENT NUMBER:

140:339334

TITLE:

Preparation of benzo[e][1,4]oxazino[3,2-g]isoindoles as antitumor agents for treating leukemia and solid tumors

INVENTOR(S):

Coudert, Gerard; Lepifre, Franck; Caignard, Daniel; Henri, Renaud; Pierre, Hickman; John; Pierre, Alain; Kraus, Berthier Laurence

PATENT ASSIGNEE(S):

Les Laboratoires Servier, Fr.

SOURCE:

Fr. Demande, 43 pp.

DOCUMENT TYPE:

CODEN: FRXXBL

LANGUAGE:

Patent

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|---------------------------|
| FR 2845994 | A1 | 20040423 | FR 2002-12964 | 20021018 |
| FR 2845994 | B1 | 20060519 | | |
| CA 2502484 | A1 | 20040506 | CA 2003-2502484 | 20031017 |
| WO 2004037830 | A1 | 20040506 | WO 2003-FR3068 | 20031017 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RM: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TO | | | | |
| AU 2003301531 | A1 | 20040513 | AU 2003-301531 | 20031017 |
| EP 1556387 | A1 | 20050727 | EP 2003-809362 | 20031017 |
| EP 1556387 | B1 | 20070404 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003014877 | A | 20050802 | BR 2003-14877 | 20031017 |
| CN 1705669 | A | 20051207 | CN 2003-80101582 | 20031017 |
| JP 20060506375 | T | 20060223 | JP 2004-546097 | 20031017 |
| AT 358677 | T | 20070415 | AT 2003-809362 | 20031017 |
| US 2006003997 | A1 | 20060105 | US 2005-531648 | 20050415 |
| NO 2005002373 | A | 20050513 | NO 2005-2373 | 20050513 |
| PRIORITY APPLN. INFO.: | | | | FR 2002-12964 A 20021018 |
| | | | | WO 2003-FR3068 W 20031017 |

OTHER SOURCE(S):

MARPAT 140:339334

OI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

AB

Title compds. I [wherein CMC = Ph, pyridinyl; Z = H, halo, aryl/alkyl aryl, aryloxy, OH and derivs.; R1 = H, aryl/alkyl, aryl, CHO and derivs., (un)substituted alkylene; R2 = H, aryl/alkyl, aryl, S(O)tH, (un)substituted alkylene; t = 0-2; R3, R4 = independently H, aryl/alkyl, aryl, or R3R4N = 5 or 6-membered ring heterocycle; n = 1-6; their enantiomers, diastereomers, N-oxides, and their salts of addition with a pharmaceutically acceptable acid or base] were prepared as antitumor agents.

Thus, tert-Bu 2,3-dihydro-4H-1,4-benzoxazin-3-one-4-carboxylate reacted with 8-(Pinacolboronyl)-1,4-dioxaspiro[4.5]dec-7-ene, followed by cycloaddn. with di-Me acetylenedicarboxylate, reduction, and deprotection to give the ketone II. Boc-protection of the enol, dehydrogenation in the presence of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, O-Boc-deprotection,

cyclocondensation with N,N-dimethylethylenediamine, and

N-Boc-deprotection

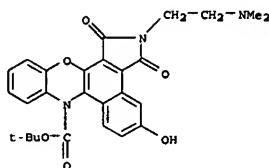
in the presence of HCl gave the hydrochloride III·HCl. III·HCl displayed an IC50 < 1 μM for inhibition of certain human cell proliferation. I are useful for treating leukemia and solid neoplasm.

680596-80-9P 680596-89-8P 680596-91-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(antitumor agent; preparation of
benzo[e][1,4]oxazino[3,2-g]isoindoles as
antitumor agents for treating leukemia and solid tumors)

RN 680596-80-9 CAPLUS

CN Benzo[a]pyrrolo[3,4-c]phenoxazine-8(1H)-carboxylic acid, 2-[2-(dimethylamino)ethyl]-2,3-dihydro-5-(2-hydroxyethoxy)-1,3-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

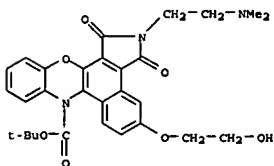


RN 680596-89-8 CAPLUS

CN Benzo[a]pyrrolo[3,4-c]phenoxazine-8(1H)-carboxylic acid, 2-[2-(dimethylamino)ethyl]-2,3-dihydro-5-(2-hydroxyethoxy)-1,3-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

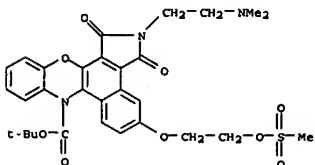
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS ON STN

(Continued)



RN 680596-91-2 CAPLUS

CN Benzo[a]pyrrolo[3,4-c]phenoxazine-8(1H)-carboxylic acid, 2-[2-(dimethylamino)ethyl]-2,3-dihydro-5-[2-[(methylsulfonyl)oxy]ethoxy]-1,3-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT 680596-88-7P 680596-92-3P 680596-93-4P,
2-(2-(Dimethylamino)ethyl)-5-(2-hydroxyethoxy)benzo[a]pyrrolo[3,4-c]phenoxazine-1,3-dione 680596-94-5P, 8-(Formyl)-2-[2-

(dimethylamino)ethyl]-5-(2-hydroxyethoxy)benzo[a]pyrrolo[3,4-c]phenoxazine-1,3-dione 680596-98-9P 680596-99-0P
680597-00-6P 680597-01-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

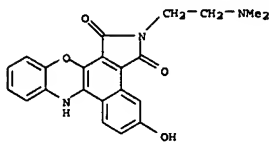
(antitumor agent; preparation of
benzo[e][1,4]oxazino[3,2-g]isoindoles as
antitumor agents for treating leukemia and solid tumors)

RN 680596-88-7 CAPLUS

CN Benzo[a]pyrrolo[3,4-c]phenoxazine-1,3(2H,8H)-dione, 2-[2-(dimethylamino)ethyl]-5-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS ON STN

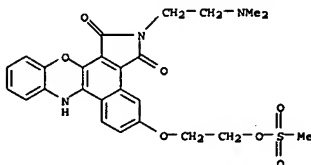
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● HCl

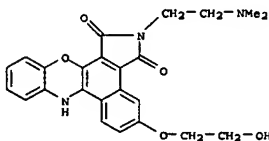
RN 680596-92-3 CAPLUS

CN Benzo[a]pyrrolo[3,4-c]phenoxazine-1,3(2H,8H)-dione, 2-[2-(dimethylamino)ethyl]-5-[2-[(methylsulfonyl)oxy]ethoxy]- (9CI) (CA INDEX NAME)



RN 680596-93-4 CAPLUS

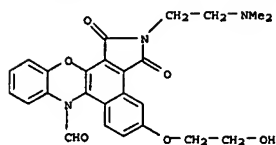
CN Benzo[a]pyrrolo[3,4-c]phenoxazine-1,3(2H,8H)-dione, 2-[2-(dimethylamino)ethyl]-5-(2-hydroxyethoxy)- (9CI) (CA INDEX NAME)



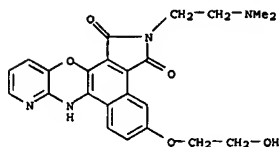
RN 680596-94-5 CAPLUS

CN Benzo[a]pyrrolo[3,4-c]phenoxazine-8(1H)-carboxaldehyde, 2-[2-(dimethylamino)ethyl]-2,3-dihydro-5-(2-hydroxyethoxy)-1,3-dioxo- (9CI) (CA INDEX NAME)

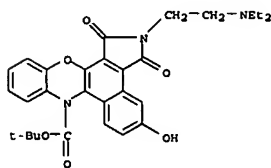
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 680596-98-9 CAPLUS
CN Benzo[6]pyrido[3,2-b]pyrrolo[3,4-h][1,4]benzoxazine-1,3(2H,8H)-dione, 2-[2-(dimethylamino)ethyl]-5-(2-hydroxyethoxy)- (9CI) (CA INDEX NAME)

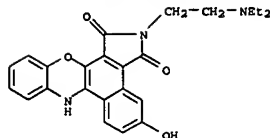


RN 680596-99-0 CAPLUS
CN Benzo[6]pyrido[3,2-b]pyrrolo[3,4-h][1,4]benzoxazine-1,3(2H,8H)-dione, 2-[2-(diethylamino)ethyl]-2,3-dihydro-5-hydroxy-1,3-dioxo-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

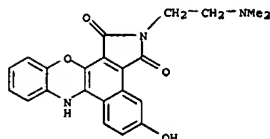


RN 680597-00-6 CAPLUS
CN Benzo[6]pyrido[3,2-b]pyrrolo[3,4-h][1,4]benzoxazine-1,3(2H,8H)-dione, 2-[2-(diethylamino)ethyl]-5-hydroxy- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 680597-01-7 CAPLUS
CN Benzo[6]pyrido[3,2-b]pyrrolo[3,4-h][1,4]benzoxazine-1,3(2H,8H)-dione, 2-[2-(dimethylamino)ethyl]-5-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT